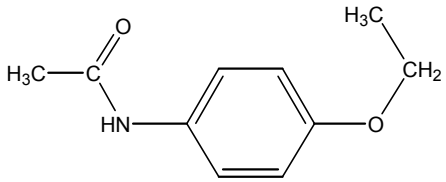
PHENACETIN
CAS No. 62-44-2
First Listed in the *First Annual Report on Carcinogens*



CARCINOGENICITY

Phenacetin is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC S.4, 1982; IARC S.7, 1987). When administered in the diet, phenacetin induced benign and malignant tumors of the urinary tract of mice and rats of both sexes and of the nasal cavity in rats of both sexes.

There is limited evidence for the carcinogenicity of phenacetin in humans (IARC S.4, 1982; IARC S.7, 1987). There are many case reports of renal pelvic cancer associated with abuse of analgesic mixtures containing phenacetin (IARC V.13, 1977; IARC V.24, 1980). Analgesic mixtures containing phenacetin are included separately in the *Eighth Report on Carcinogens*, Section III.A.

PROPERTIES

Phenacetin occurs as a white, odorless, crystalline powder or as white, glistening, crystalline scales. It is slightly soluble in water, ethanol, chloroform, and diethyl ether, and slightly soluble in glycerol. When heated to decomposition, phenacetin emits toxic fumes of nitrogen oxides (NO_x). Phenacetin has been available in the United States as a grade containing 98%-101% active ingredient on a dried basis with a maximum of 0.03% *p*-chloroacetanilide, and in 300-mg doses as tablets containing 94%-106% of the stated amount of phenacetin. Various mixtures containing phenacetin were previously available.

USE

Phenacetin is used as an analgesic and antipyretic drug for humans and animals. It is used alone or previously in combination with aspirin and caffeine, for the relief of mild-to-moderate muscle pain. Phenacetin also has been used as a stabilizer for hydrogen peroxide in hair-bleaching preparations (IARC V.24, 1980).

PRODUCTION

The USITC does not currently identify any producers or production volumes for phenacetin. In 1985, 58,000 lb of phenacetin were imported (USDOC Imports, 1986). There was one domestic firm producing undisclosed volumes of phenacetin in 1979 and 1980 (USITC, 1980; USITC, 1981). U.S. imports of phenacetin exceeded 82,000 lb in 1987 (USDOC Imports, 1988). The 1979 TSCA Inventory identified two companies producing 550,000 lb of phenacetin,

and five firms importing 55,000 lb in 1977 (TSCA, 1979). Phenacetin was first produced domestically in the 1920s (IARC V.13, 1977).

EXPOSURE

The primary routes of potential human exposure to phenacetin are ingestion, inhalation, and dermal contact. Phenacetin was previously formulated with other pharmaceutical agents and used in over-the-counter remedies for pain and fever. The usual dosage was 300 mg 4-6 times per day not exceeding 2 g (IARC V.13, 1977). Potential occupational exposure may occur through inhalation and dermal contact for workers involved in the manufacture, formulation, packaging, or administration of phenacetin. The National Occupational Exposure Survey (1981-1983) indicates that 17,408 total workers, including 14,497 women, potentially were exposed to phenacetin (NIOSH, 1984). The National Occupational Hazard Survey, conducted by NIOSH from 1972 to 1974, estimated that 4,186 workers were potentially exposed to phenacetin in the workplace in 1970 (NIOSH, 1976). Its half-life in air is <1 day and in water > 30 days.

REGULATIONS

EPA regulates phenacetin under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) and the Resource Conservation and Recovery Act (RCRA). A reportable quantity (RQ) of 100 lb has been proposed for phenacetin under CERCLA. This compound is regulated as a hazardous waste and is subject to report and recordkeeping requirements under RCRA. After an advisory panel determined that phenacetin could not be considered "safe" for over-the-counter (OTC) use, FDA held hearings to remove it from OTC and prescription products. FDA has withdrawn approval of all drugs containing phenacetin and has required manufacturers to reformulate them to omit phenacetin. OSHA regulates phenacetin under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-117.